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# Unexpected formation of 10-iodo- and 10-chlorocamphor under halosulfonylation conditions, and convenient routes to 10-chloro- and 10-bromocamphor

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**Abstract**—Generation of camphor-10-sulfonyl iodide *in situ* under halosulfonylation conditions or exposure of camphor-10-sulfonyl chloride to copper (II) chloride under Asscher-Vofsi conditions unexpectedly leads to the formation of 10-iodocamphor or 10-chlorocamphor respectively. Additionally, convenient syntheses of 10-bromocamphor and 10-chlorocamphor have been achieved by extension of previously reported methodology. © 2013 Elsevier Science. All rights reserved

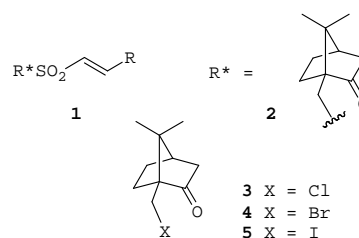
## 1. Introduction

Unsaturated sulfones have found widespread use as versatile intermediates in organic synthesis, especially as Michael acceptors and in cycloaddition reactions.<sup>1,2</sup> However, there do not appear to have been any reports of either the synthesis or applications of vinylic sulfones **1** which possess homochiral alkyl groups R\* that are directly attached to the sulfur atom. The conformationally rigid, monoterpene-based camphorsulfonyl framework **2** (Figure 1), which is already widely exploited as a component of various practical chiral auxiliaries,<sup>3</sup> and which is readily available in both enantiomeric forms, seemed to be a promising candidate for this purpose. In this paper, we describe the unexpected formation of 10-halocamphors **3–5** (X = Cl/Br/I) during attempted halosulfonylation reactions of some alkenes, and show how these versatile chiral synthons can be readily accessed from (+)-camphor-10-sulfonic acid.

## 2. Results and Discussion

During the course of our ongoing work on the development of sulfonyl-based chiral auxiliaries, we sought to synthesize various chiral vinyl sulfones *via* halosulfonylation reactions of alkenes. Initially, we opted to generate camphor-10-sulfonyl iodide **7** *in situ* in the immediate presence of an alkene, by treating sodium (+)-camphor-10-sulfinate **6** (available by reduction of (+)-camphor-10-sulfonyl

chloride)<sup>4</sup> with iodine, a strategy successfully utilised by others for reactions involving arenesulfonyl iodides.<sup>5</sup>

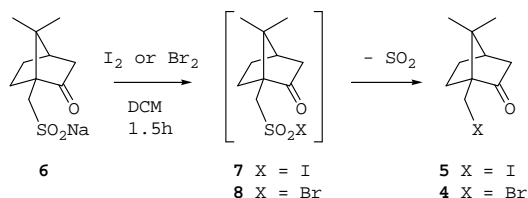


**Figure 1.** Homochiral camphor-based vinyl sulfones and the 10-halocamphors.

In the event, when an aqueous solution of sodium (+)-camphor-10-sulfinate **6** was vigorously stirred at ambient temperature with a DCM solution of iodine and allyl benzyl ether, (–)-10-iodocamphor **5** was unexpectedly formed and unchanged alkene was recovered, rather than the expected β-iodosulfone (Scheme 1). (–)-10-Iodocamphor **5** was also obtained in the absence of the alkene, and when triethylamine (normally used to generate the vinyl sulfone *in situ* from the β-iodosulfone) was added before work-up. On the other hand, when either norbornene or 1,5-cyclooctadiene was the alkene, reaction with sodium (+)-camphorsulfinate **6** and iodine in methanol as solvent, followed by *in situ* treatment with potassium *tert*-butoxide did afford the expected vinylic sulfones, albeit in only modest yields.<sup>6</sup>

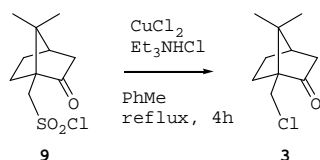
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We next showed that reaction of sodium (+)-camphor-10-sulfinate **6** with bromine in DCM solution formed the sulfonyl bromide **8**, which could be converted into (+)-10-bromocamphor **4**. This required the thermolysis of crude **8** in either refluxing xylene or toluene, demonstrating its greater stability over that of the sulfonyl iodide **7**.



**Scheme 1.**

These results prompted us to investigate the addition of (+)-camphor-10-sulfonyl chloride **9** to alkenes under free-radical conditions. Asscher and Vofsi have described how the radical addition of arenesulfonyl chlorides to alkenes can be conveniently catalysed by the system  $\text{CuCl}_2 - \text{Et}_3\text{N} \cdot \text{HCl}$  in refluxing toluene.<sup>7</sup> However, when 1,5-cyclooctadiene was reacted with (+)-camphor-10-sulfonyl chloride **9** under these conditions none of the anticipated adduct was formed. Instead, the alkene was recovered and (+)-10-chlorocamphor **3** was obtained in excellent yield (Scheme 2). The same product **3** was efficiently formed in the absence of alkene, but it was not obtained in the absence of the  $\text{Cu(II)}$  catalyst. Other simple cycloalkenes such as cyclohexene also failed to yield radical addition products under Asscher-Vofsi conditions.

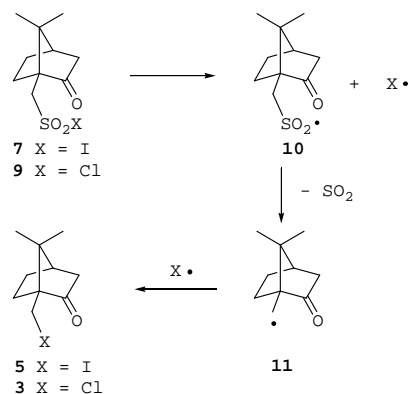


**Scheme 2.**

From the above results, we conclude that homolytic fission of the sulfonyl halides **7** or **9** leads to the rather hindered, neopentyl-like, sulfonyl radical **10** which loses sulfur dioxide<sup>8</sup> to form the 10-camphoryl radical **11** more rapidly than it can react with an alkene. Recombination of **11** with either an iodine or chlorine atom then yields either (-)-10-iodocamphor **5** or (+)-10-chlorocamphor **3**, respectively (Scheme 3). The failure of the sulfonyl halides **7** and **9** to form adducts with alkenes is perhaps not too surprising, given that analogous aliphatic alkanesulfonyl iodides are unstable and decompose with loss of sulfur dioxide.<sup>9</sup>

The 10-halocamphors **3**, **4** and **5** have been widely used both as sources of chirality in asymmetric synthesis, and as precursors to chiral synthons employed in total synthesis. Both (+)-10-bromocamphor **4** and (-)-10-iodocamphor **5** have been converted into various homochiral bidentate P-P, N-P and N-S donor ligands for asymmetric synthesis.<sup>10</sup> Chiral imidazolium-based ionic liquids,<sup>11</sup> telluronium salts<sup>12</sup> and ligands for asymmetric Pauson-Khand

reactions<sup>13</sup> have been derived from (-)-10-iodocamphor **5**, whilst chiral Brønsted acids have been synthesized from (+)-10-bromocamphor **4**.<sup>14</sup> Additionally, fragmentation of the C(1)-C(2) bond in **4** and **5** affords chiral cyclopentenones<sup>15</sup> which have been utilised as chiral synthons in the total synthesis of various natural products.<sup>16</sup>



**Scheme 3.**

(+)-10-Chlorocamphor **3** has previously been obtained from “oxy-camphene”,<sup>17</sup> by the oxidation of 10-chloroisoborneol,<sup>18</sup> by the reduction of 8-bromo-3,10-dichlorocamphor using zinc in acetic acid,<sup>19</sup> by triflic anhydride-promoted Wagner-Meerwein rearrangement of (+)-camphor<sup>20</sup> and by prolonged reaction of (+)-10-bromocamphor **4** with  $\text{LiCl}$  in DMF.<sup>21</sup> Although the facile and direct route to (+)-10-chlorocamphor **3** from (+)-camphor-10-sulfonyl chloride **9** via the method described above makes this a more readily accessible chiral synthon, more efficient routes exist for the preparation of (+)-10-bromocamphor **4** and (-)-10-iodocamphor **5** which can both be accessed from (+)-camphor in 3-steps via the above-mentioned Wagner-Meerwein rearrangement<sup>20</sup> or, in the case of (+)-10-bromocamphor **4**, by thermolysis of (+)-camphor-10-sulfonyl bromide **8**.<sup>22</sup>

A convenient synthesis of (-)-10-iodocamphor **5** directly from commercially available (+)-camphor-10-sulfonic acid via reduction with  $\text{I}_2/\text{PPh}_3$  has been previously reported,<sup>23</sup> although to the best of our knowledge this methodology has not been previously applied to the synthesis of either **3** or **4**. Given the widespread use of the 10-halocamphors **3**, **4** and **5** as chiral synthons, we sought to extend this methodology to the synthesis of both (+)-10-bromocamphor **4** and (+)-10-chlorocamphor **3** by appropriate choice of electrophilic halogenating reagent. These results are summarised in Table 1.

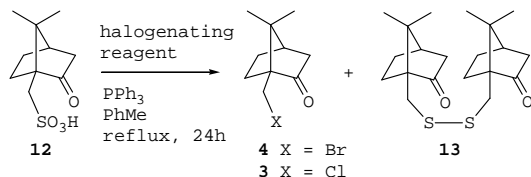
Reduction of (+)-camphor-10-sulfonic acid **12** with bromine (3 equivalents) and triphenylphosphine (5 equivalents) in refluxing toluene gave (+)-10-bromocamphor **4** in 78 % yield after purification by chromatography. Encouraged by this result, we examined various halogen donors and found that both carbon tetrabromide and *N*-bromosuccinimide were also suitable reagents for the preparation of **4**.

**Table 1.** Synthesis of **4** and **3** via reduction of (+)-camphor-10-sulfonic acid **12** with PPh<sub>3</sub> and various halogenating reagents.

Entry	Reagent (equiv)	PPh <sub>3</sub> (equiv)	Bu <sub>3</sub> N (equiv)	Ratio of <b>3</b> or <b>4</b> : <b>13</b> <sup>a</sup>	Yield of <b>3</b> or <b>4</b> (%) <sup>b</sup>	Yield of <b>13</b> (%) <sup>b</sup>
1	Br <sub>2</sub> (3)	(5)	(0)	1:0 <sup>c</sup>	78 ( <b>4</b> )	0
2	NBS (3)	(5)	(0)	1.5:1	44 ( <b>4</b> )	30
3	CBr <sub>4</sub> (3)	(5)	(0)	1.9:1	50 ( <b>4</b> )	27
4	CBr <sub>4</sub> (4)	(6)	(1)	1:0 <sup>c</sup>	84 ( <b>4</b> )	0
5	C <sub>2</sub> Cl <sub>6</sub> (3)	(5)	(0)	3.4:1	68 ( <b>3</b> )	18
6	NCS (3)	(5)	(0)	3.7:1	70 ( <b>3</b> )	17
7	CCl <sub>4</sub> (3)	(5)	(0)	3:1	66 ( <b>3</b> )	20
8	CCl <sub>4</sub> (3)	(5)	(0)	4.1:1 <sup>d</sup>	68 ( <b>3</b> )	15
9	CCl <sub>4</sub> (4)	(6)	(0)	6.2:1	72 ( <b>3</b> )	11
10	CCl <sub>4</sub> (5)	(7)	(0)	5.8:1	69 ( <b>3</b> )	13
11	CCl <sub>4</sub> (4)	(6)	(1)	30:1	81 ( <b>3</b> )	3

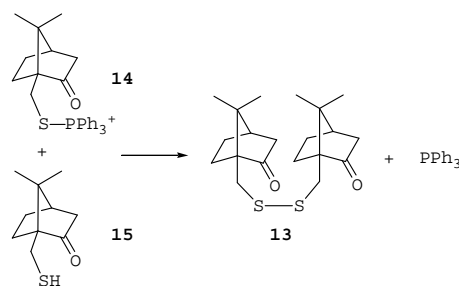
<sup>a</sup>Determined by <sup>1</sup>H NMR. <sup>b</sup>Isolated yield.<sup>c</sup>Disulfide **13** not detected. <sup>d</sup>Reaction time was 48 hours.

Similarly, carbon tetrachloride, hexachloroethane and *N*-chlorosuccinimide could all be successfully employed for the synthesis of (+)-10-chlorocamphor **3**. However, in a number of the reduction experiments bis(10-camphoryl) disulfide **13**<sup>24</sup> was also obtained in variable quantities as by-product in addition to the desired 10-halocamphor **3** or **4** (Scheme 4).

**Scheme 4.**

By consideration of the mechanism of the analogous reduction of acid **12** with I<sub>2</sub>/PPh<sub>3</sub>,<sup>23</sup> we attribute the formation of disulfide **13** to the competitive trapping of mercaptotriphenylphosphonium ion **14** with 10-mercaptocamphor **15**,<sup>25</sup> rather than with bromide ion or (the somewhat less nucleophilic) chloride ion (Scheme 5). In order to minimize the formation of disulfide **13** and improve the yields of the desired 10-halocamphor **3** or **4**, we briefly examined the influence of reaction stoichiometry, reaction time and the addition of base on the yields of **3** and **4**.

It was found that prolonging the reaction time (entry 8), or the use of additional equivalents of both the halogenating reagent and triphenylphosphine (entries 9 and 10) led to only a modest improvement in the yield of **3**. The best results were obtained when tributylamine (1 equivalent) was added to the reaction mixture<sup>23</sup> prior to reflux. Under these conditions (+)-10-chlorocamphor **3** and (+)-10-bromocamphor **4** were obtained in improved yields of 81 % (entry 11) and 84 % (entry 4), respectively.

**Scheme 5.**

### 3. Conclusion

It has been found that camphor-10-sulfonyl iodide **7**, formed *in situ* from sodium (+)-camphor-10-sulfinate **6**, undergoes spontaneous and efficient conversion into (–)-10-iodocamphor **5**. Similarly, exposure of (+)-camphor-10-sulfonyl chloride **9** to Asscher-Vofsi radical conditions generates (+)-10-chlorocamphor **3** in high yield. Failure to effect the halosulfonylation of alkenes under these conditions may be attributed to the competing rapid extrusion of sulfur dioxide from the sterically hindered camphorsulfonyl radical **10**. In addition, a previously reported synthesis of (–)-10-iodocamphor **5** has been extended to deliver both (+)-10-chlorocamphor **3** and (+)-10-bromocamphor **4**, leading to convenient syntheses of these important chiral synthons directly from commercially available (+)-camphor-10-sulfonic acid **12**.

### 4. Experimental

#### 4.1. General

NMR spectra were recorded using a Bruker AVANCE DPX 400 MHz spectrometer (400.1 MHz for <sup>1</sup>H and 100.6 MHz for <sup>13</sup>C). Chemical shifts are reported in parts per million. Coupling constants (*J*) are quoted in Hertz. Optical rotations were measured using a Perkin-Elmer 141 polarimeter. IR spectra were recorded for Nujol mulls (N) on a Mattson Genesis II FTIR spectrometer. Mass spectra were obtained under electrospray conditions using a Micromass LCT instrument. All solvents and reagents were purified by standard techniques. Organic extracts of reaction products were dried over anhydrous magnesium sulfate.

#### 4.2. (1*S*,4*R*)-(7,7-Dimethyl-2-oxobicyclo[2.2.1]hept-1-yl) methanesulfonyl chloride **9**.

Thionyl chloride (37.7 mL, 516 mmol) was added to (+)-camphor-10-sulfonic acid **12** (40.0 g, 172 mmol) in a 1L flask. The mixture was stirred at room temperature for 1 hr, warmed at 40 °C for a further 6 hrs and then cooled back to room temperature and left stirring overnight. The mixture was diluted with ether (400 mL) and quenched over ice/H<sub>2</sub>O. The aqueous layer was extracted with ether (400 mL). The combined organic extracts were washed with water (200 mL) and saturated sodium hydrogen carbonate

solution (4 × 100 mL) until the evolution of CO<sub>2</sub> had ceased, and then dried and evaporated to afford (+)-camphor-10-sulfonyl chloride **9** as a white solid (38.0 g, 89 %); Mp 62–63 °C (ether); Lit.<sup>26</sup>: 67–68 °C. [ $\alpha$ ]<sub>D</sub> = +30.9 (*c* 1.29, CHCl<sub>3</sub>, 27 °C); Lit.<sup>27</sup>: +28.8 (*c* 4.2, CHCl<sub>3</sub>). IR:  $\nu_{\text{max}}$  (N) 2921, 1741 (C=O), 1459, 1368, 1279, 1171, 1132, 1102, 1045 (SO<sub>2</sub>), 854, 768 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 0.94 (s, 3H, 7-CH<sub>3</sub>), 1.16 (s, 3H, 7-CH<sub>3</sub>), 1.47–1.54 (m, 1H), 1.76–1.83 (m, 1H), 2.01 (d, *J* = 18.4, 1H, 3-CH<sub>2</sub> *endo*), 2.08–2.16 (m, 1H), 2.18 (t, *J* = 4.7, 1H, 4-CH), 2.42–2.52 (m, 2H), 3.74 (d, *J* = 14.3, 1H, CH<sub>2</sub>SO<sub>2</sub>Cl), 4.32 (d, *J* = 14.3, 1H, CH<sub>2</sub>SO<sub>2</sub>Cl). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 19.2 (7-CH<sub>3</sub>), 19.3 (7-CH<sub>3</sub>), 24.8 (C-5), 26.4 (C-6), 41.8 (C-3), 42.3 (C-4), 47.7 (C-7), 59.2 (C-1), 63.7 (CH<sub>2</sub>SO<sub>2</sub>Cl), 212.3 (C-2).

#### 4.3. Sodium (1*S*,4*R*)-(7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl)methanesulfinate **6**.

(+)-Camphor-10-sulfonyl chloride **9** (36.3 g, 144 mmol) in dry acetone (80 mL) was added dropwise over 4 hrs to a solution of sodium sulfite (35.29 g, 280 mmol) and sodium hydrogen carbonate (23.52 g, 280 mmol) in water (200 mL) maintained at 70 °C. The mixture was stirred for an additional 1 hr at 70 °C and was then allowed to cool to room temperature and left stirring overnight. The mixture was evaporated to yield a white residue which was taken up in boiling methanol (ca. 100 mL) and filtered through celite. The filtrate was evaporated to afford sodium sulfinate **6** as a white solid (31.43 g, 94 %) together with ca. 5 % (<sup>1</sup>H NMR) of the corresponding sodium sulfonate. This was used without further purification; [ $\alpha$ ]<sub>D</sub> = -41.8 (*c* 0.76, H<sub>2</sub>O, 22 °C); Lit.<sup>26</sup>: -58.2 (*c* 0.885, H<sub>2</sub>O, 19 °C). IR:  $\nu_{\text{max}}$  (N) 3358, 2918, 1741 (C=O), 1460, 1375, 1278, 1197, 1020, 973, (S=O), 851, 816, 723 cm<sup>-1</sup>. <sup>1</sup>H NMR (D<sub>2</sub>O): 0.80 (s, 3H, 7-CH<sub>3</sub>), 0.93 (s, 3H, 7-CH<sub>3</sub>), 1.33–1.40 (m, 1H), 1.43–1.51 (m, 1H), 1.88 (d, *J* = 19.0, 1H, 3-CH<sub>2</sub> *endo*), 1.92–2.00 (m, 1H), 2.00–2.06 (dd, *J* = 12.0, 2.5, 1H), 2.10 (t, *J* = 4.5, 1H, 4-CH), 2.13 (d, *J* = 13.5, 1H, CH<sub>2</sub>SO<sub>2</sub>Na), 2.35–2.42 (ddd, *J* = 19.0, 4.5, 3.0, 1H, 3-CH<sub>2</sub> *exo*), 2.57 (d, *J* = 13.5, 1H, CH<sub>2</sub>SO<sub>2</sub>Na). <sup>13</sup>C NMR (D<sub>2</sub>O): 18.3 (7-CH<sub>3</sub>), 18.7 (7-CH<sub>3</sub>), 25.6 (C-5), 25.9 (C-6), 42.0 (C-4), 42.3 (C-3), 47.6 (C-7), 58.5 (C-1), 59.5 (CH<sub>2</sub>SO<sub>2</sub>Na), 223.8 (C-2).

#### 4.4. (1*S*,4*R*)-1-(Iodomethyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one **5**.

A solution of iodine (0.5 g, 1.97 mmol) in DCM (100 mL) was vigorously mixed with a solution of sodium sulfinate **6** (0.54 g, 2.16 mmol) in water (50 mL) in a separating funnel. The yellow organic phase was placed in a round bottomed flask and stirred at room temperature for 1.5 hrs. The solution was then washed with water (50 mL) and the aqueous layer was extracted with ether (50 mL). The combined organic extracts were washed with saturated aqueous sodium sulfite (50 mL), dried and evaporated to afford (-)-10-iodocamphor **5** as a white solid (0.36 g, 65 %); Mp 69 °C (DCM); Lit.<sup>28</sup>: 71 °C. [ $\alpha$ ]<sub>D</sub> = -20.1 (*c* 1.28, CHCl<sub>3</sub>, 23 °C); Lit.<sup>28</sup>: -20.4 (*c* 1, CHCl<sub>3</sub>, 23 °C). IR  $\nu_{\text{max}}$  (N) 2921, 1743 (C=O), 1456, 1417, 1375, 1297, 1213, 1188, 1163, 1063, 1038, 955, 891, 766 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 0.91 (s, 3H, 7-CH<sub>3</sub>), 1.08 (s, 3H, 7-CH<sub>3</sub>), 1.40 (t,

*J* = 9.5, 1H, 5-CH<sub>2</sub> *endo*), 1.62 (t, *J* = 9.5, 1H, 6-CH<sub>2</sub> *endo*), 1.92 (d, *J* = 18.5, 1H, 3-CH<sub>2</sub> *endo*), 1.96–2.05 (m, 2H, 5-CH<sub>2</sub> *exo* and 6-CH<sub>2</sub> *exo*), 2.17 (app dd, *J* = 5.5, 2.5, 1H, 4-CH), 2.41 (ddd, *J* = 18.5, 5.0, 2.0, 1H, 3-CH<sub>2</sub> *exo*), 3.13 (d, *J* = 11.0, 1H, CH<sub>2</sub>I), 3.32 (d, *J* = 11.0, 1H, CH<sub>2</sub>I). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 0.3 (CH<sub>2</sub>I), 19.6 (7-CH<sub>3</sub>), 19.8 (7-CH<sub>3</sub>), 26.2 (C-5), 30.0 (C-6), 42.5 (C-3), 43.5 (C-4), 47.8 (C-7), 58.6 (C-1), 214.7 (C-2). HRMS (EI, MeOH): *m/z* calcd for C<sub>10</sub>H<sub>15</sub>OI [M + Na]<sup>+</sup>: 301.0064; found: 301.0077.

#### 4.5. (1*S*,4*R*)-1-(Bromomethyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one **4**.

##### 4.5.1. Method A: From Sodium Sulfinate **6**.

A solution of bromine (0.1 mL, 1.97 mmol) in DCM (100 mL) was vigorously mixed with a solution of sodium sulfinate **6** (0.54 g, 2.16 mmol) in water (50 mL) in a separating funnel. The organic phase was removed and evaporated and the resulting solid was dissolved in xylene (15 mL). The solution was heated under reflux for 6 hrs. The solution was allowed to cool to room temperature, water (50 mL) was added and the mixture was extracted with ether (3 × 50 mL). The combined organic extracts were dried and evaporated to yield an oil which was purified by column chromatography on silica gel, eluting with ether/hexane (1:10) to afford (+)-10-bromocamphor **4** as a white solid (0.33 g, 72 %).

##### 4.5.2. Method B: From Sulfonic Acid **12**.

(+)-Camphor-10-sulfonic acid **12** (1.00 g, 4.30 mmol) and triphenylphosphine (6.77 g, 25.82 mmol) were dissolved in dry toluene (30 mL) under an atmosphere of nitrogen. Solid carbon tetrabromide (5.71 g, 17.21 mmol) was added, followed by tributylamine (1.02 mL, 4.30 mmol) and the solution was heated under reflux for 24 hrs. The solution was then allowed to cool to room temperature and water (50 mL) was added. The phases were mixed and separated and the aqueous phase was extracted with DCM (2 × 50 mL). The combined organic extracts were washed with water (50 mL), dried and evaporated to afford a brown solid (12.59 g) which was triturated with ether (ca. 20 mL) and filtered. The filtrate was evaporated to yield a brown solid which was purified by column chromatography on silica gel, eluting with ether/hexane (1:10) to afford (+)-10-bromocamphor **4** as a white solid (0.83 g, 84 %); Mp 75 °C (ether/hexane); Lit.<sup>29</sup>: 76–77 °C. [ $\alpha$ ]<sub>D</sub> = +24.8 (*c* 1.12, CHCl<sub>3</sub>, 23 °C); Lit.<sup>28</sup>: +25.7 (*c* 1, CHCl<sub>3</sub>, 23 °C). IR  $\nu_{\text{max}}$  (N) 2923, 2854, 1747 (C=O), 1457, 1375, 1328, 1275, 1234, 1165, 1066, 1044, 963, 906, 851, 774, 706, 669, 634 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 0.96 (s, 3H, 7-CH<sub>3</sub>), 1.12 (s, 3H, 7-CH<sub>3</sub>), 1.40–1.46 (m, 1H, 5-CH<sub>2</sub> *endo*), 1.54–1.61 (m, 1H, 6-CH<sub>2</sub> *endo*), 1.93 (d, *J* = 18.5, 1H, 3-CH<sub>2</sub> *endo*), 2.00–2.08 (m, 1H), 2.11–2.15 (m, 1H), 2.12 (t, *J* = 4.0, 1H, 4-CH), 2.43 (dt, *J* = 18.5, 4.0, 1H, 3-CH<sub>2</sub> *exo*), 3.42 (d, *J* = 11.5, 1H, CH<sub>2</sub>Br), 3.64 (d, *J* = 11.5, 1H, CH<sub>2</sub>Br). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 19.8 (7-CH<sub>3</sub>), 20.0 (7-CH<sub>3</sub>), 26.2 (C-5), 27.2 (C-6), 28.9 (CH<sub>2</sub>Br), 42.5 (C-3), 43.4 (C-4), 47.8 (C-7), 59.8 (C-1), 215.1 (C-2). HRMS (EI, MeOH) *m/z* calcd for C<sub>10</sub>H<sub>15</sub>OBr [M + Na]<sup>+</sup>: 253.0203; found: 253.0200.

#### 4.6. (1S,4R)-1-(Chloromethyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one 3.

##### 4.6.1. Method A: From Sulfonyl Chloride 9.

Copper (II) chloride (0.02 g, 1.24 mol %) and triethylammonium chloride (0.03 g, 1.82 mol %) were added to a solution of (+)-camphor-10-sulfonyl chloride **9** (3.0 g, 11.96 mmol) in dry toluene (15 mL). The resulting mixture was heated under nitrogen at 110 °C during 4 hrs. The solvent was removed under reduced pressure and the residue was taken up in DCM (30 mL). The catalyst system was then precipitated using methanol (5 mL) and the organic layer was filtered and washed with 10 % sodium hydrogen carbonate solution (20 mL) and with water (20 mL). The extract was dried and evaporated under reduced pressure to afford (+)-10-chlorocamphor **3** as a white solid (2.19 g, 89 %) which was recrystallised from methanol.

##### 4.6.2. Method B: From Sulfonic Acid 12.

(+)-Camphor-10-sulfonic acid **12** (1.00 g, 4.30 mmol) and triphenylphosphine (6.77 g, 25.82 mmol) were dissolved in dry toluene (30 mL) under an atmosphere of nitrogen. Carbon tetrachloride (1.66 mL, 17.21 mmol) was added dropwise *via* syringe, followed by tributylamine (1.02 mL, 4.30 mmol) and the solution was heated under reflux for 24 hrs. The solution was then allowed to cool to room temperature and water (50 mL) was added. The phases were mixed and separated and the aqueous phase was extracted with DCM (2 × 50 mL). The combined organic extracts were washed with water (50 mL), dried and evaporated to afford a brown solid (8.70 g) which was triturated with ether (ca. 20 mL) and filtered. The filtrate was evaporated to yield a brown solid which was purified by column chromatography on silica gel, eluting with ether/hexane (1:10) to afford two products. The first product to elute was (+)-10-chlorocamphor **3** as a white solid (0.65 g, 81 %); Mp 129 °C (ether/hexane); Lit.<sup>21</sup>: 131–132 °C.  $[\alpha]_D^{25} = +39.7$  (c 1.16, EtOH, 16 °C); Lit.<sup>21</sup>: +41.8 (c 0.96, EtOH, 20 °C). IR  $\nu_{\max}$  (N) 2925, 1744 (C=O), 1455, 1414, 1375, 1301, 1219, 1168, 1101, 1053, 1006, 982, 934, 853, 762, 716, 639  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ): 0.99 (s, 3H, 7- $\text{CH}_3$ ), 1.13 (s, 3H, 7- $\text{CH}_3$ ), 1.39–1.46 (m, 1H, 5- $\text{CH}_2$  *endo*), 1.48–1.54 (m, 1H, 6- $\text{CH}_2$  *endo*), 1.92 (d,  $J = 18.5$ , 1H, 3- $\text{CH}_2$  *endo*), 2.01–2.07 (m, 1H), 2.10 (t,  $J = 4.5$ , 1H, 4- $\text{CH}$ ), 2.18 (td,  $J = 12.0$ , 4.0, 1H), 2.43 (dt,  $J = 18.5$ , 4.5, 1H, 3- $\text{CH}_2$  *exo*), 3.62 (d,  $J = 12.0$ , 1H,  $\text{CH}_2\text{Cl}$ ), 3.81 (d,  $J = 12.0$ , 1H,  $\text{CH}_2\text{Cl}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ): 19.9 (7- $\text{CH}_3$ ), 20.0 (7- $\text{CH}_3$ ), 25.6 (C-5), 26.2 (C-6), 40.9 ( $\text{CH}_2\text{Cl}$ ), 42.6 (C-3), 43.3 (C-4), 47.3 (C-7), 60.6 (C-1), 215.5 (C-2). HRMS (EI, MeOH)  $m/z$  calcd for  $\text{C}_{10}\text{H}_{15}\text{OCl}$  [ $\text{M} + \text{H}$ ]<sup>+</sup>: 187.0890; found: 187.0892. The second product to elute was bis(10-camphoryl) disulfide **13** as a white solid (0.02 g, 3 %); Mp 233–234 °C (ether/hexane); Lit.<sup>24</sup>: 236–238 °C.  $[\alpha]_D^{25} = -102.1$  (c 0.94,  $\text{CHCl}_3$ , 22 °C); Lit.<sup>24</sup>: -103.66 (c 1,  $\text{CHCl}_3$ , 25 °C). IR  $\nu_{\max}$  (N) 2927, 1738 (C=O), 1453, 1412, 1375, 1301, 1219, 1168, 1102, 1062, 1006, 982, 944, 859, 765, 711, 645  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ): 0.92 (s, 6H, 2 × 7- $\text{CH}_3$ ), 1.07 (s, 6H, 2 × 7- $\text{CH}_3$ ), 1.37–1.46 (m, 2H), 1.47–1.53 (m, 2H), 1.57–1.64 (m, 2H), 1.88 (d,  $J = 18.0$ , 2H, 2 × 3- $\text{CH}_2$

*endo*), 1.99–2.07 (m, 2H), 2.09 (t,  $J = 4.5$ , 2H, 2 × 4- $\text{CH}$ ), 2.41 (dt,  $J = 18.0$ , 4.5, 2H, 2 × 3- $\text{CH}_2$  *exo*), 2.82 (d,  $J = 13.0$ , 2H, 2 ×  $\text{CH}_2\text{S}$ ), 3.27 (d,  $J = 13.0$ , 2H, 2 ×  $\text{CH}_2\text{S}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ): 19.5 (2 × 7- $\text{CH}_3$ ), 19.7 (2 × 7- $\text{CH}_3$ ), 26.0 (2 × C-5), 26.3 (2 × C-6), 38.1 (2 ×  $\text{CH}_2\text{S}$ ), 42.5 (2 × C-3), 42.9 (2 × C-4), 47.3 (2 × C-7), 60.7 (2 × C-1), 216.5 (2 × C-2). HRMS (EI, MeOH)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{30}\text{O}_2\text{S}_2$  [ $\text{M} + \text{Na}$ ]<sup>+</sup>: 389.1584; found: 389.1531.

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